

NIAAA SPECTRUM

Volume 8, Issue 1 | February 2016 | <http://www.spectrum.niaaa.nih.gov>

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • National Institutes of Health • National Institute on Alcohol Abuse and Alcoholism

FEATURE

SEX DIFFERENCES TO BECOME FUNDAMENTAL ELEMENT OF ALCOHOL RESEARCH AT NIAAA



New Year's celebrations have come and gone, so before our resolutions to avoid harmful drinking patterns become distant memories, here are a few reminders to help keep 2016 on a healthy course:

- Moderate alcohol consumption is defined as up to 1 drink per day for women and up to 2 drinks per day for men.
- Low-risk drinking for having alcohol use disorder (AUD) for women is the consumption of no more than 3 drinks on any day and no more than 7 per week, and for men it is no more than 4 drinks on any day and no more than 14 per week.
- Binge drinking for women is having 4 or more drinks within 2 hours; for men, it is 5 or more drinks within 2 hours.

Why the different limits for women and men? And what do we really know about sex differences when it comes to alcohol consumption and alcohol effects?

"These are important questions, particularly in light of recent NIH-wide efforts to address sex differences in preclinical research," notes NIAAA Director George F. Koob, Ph.D. "Some of the basics are well-established, but animal models of alcohol addiction reveal significant differences between males and females, and we have little data thus far to help us understand those differences."

In the United States, and throughout the world, men drink more alcohol than women. But research shows that women start to have alcohol-related problems at lower drinking levels than men do. On average, women weigh less than men and also have less water in their bodies, pound for pound, than men do. So, because alcohol resides predominantly in body water, after a man and woman of the same weight drink the same amount of alcohol, the woman's blood alcohol concentration will tend to be higher, putting her at greater risk for harm from alcohol's acute effects, including accidents and injuries.

The long-term harmful health effects of alcohol are important as well. For example, women who drink are more likely to develop alcoholic hepatitis (liver inflammation) than men who drink the same amount of alcohol. Alcoholic hepatitis can lead to cirrhosis. Chronic heavy drinking (binge drinking five or more times a month) is a leading cause of heart disease, and, among heavy drinkers, women are more susceptible to alcohol-related heart disease than men, even though women drink less

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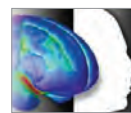
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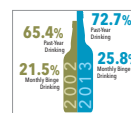
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FEATURE

DR. KENNETH WARREN RETIRES FROM NIAAA



November 1, 2015, marked a watershed moment in NIAAA's history: It was the day that Kenneth R. Warren, Ph.D., retired as Deputy Director. Dr. Warren's federal career spanned 41 years, including 39 with NIAAA. "Dr. Warren has shown incredible dedication to NIAAA, and the impact of his many accomplishments will continue long after this transition into the next phase of his life," noted NIAAA Director George F. Koob, Ph.D.

Dr. Warren's federal research career began at the Walter Reed Army Institute for Research. There, following his graduate and postdoctoral training in biochemistry, he focused on metabolic control mechanisms, including birth defects involving metabolic problems.

In 1976, Dr. Warren joined NIAAA, where he turned his attention to seminal reports about a newly described condition known as fetal alcohol syndrome (FAS). Dr. Warren was aware that the public—including the medical community—knew very little about the safety of alcohol consumption during pregnancy. Recognizing its public health ramifications, Dr. Warren pioneered NIAAA's

support for FAS research. He remains dedicated to advancing research and awareness of what today we know more broadly as fetal alcohol spectrum disorders (FASD).

Dr. Warren's early passion for FAS studies yielded groundbreaking results. In 1977, he authored the first U.S. Government health advisory on alcohol and pregnancy, and in 1981 he was the chief architect of the Surgeon General's Advisory on Alcohol Use in Pregnancy—the advisory that brought about the now-familiar warning labels

of Extramural Research. Later he was Director of the Office of Scientific Affairs as well as Executive Secretary of the Institute's National Advisory Council. Most recently, he was NIAAA Deputy Director for 7 years. He also served as NIAAA Acting Director for more than 5 years. During that time, Dr. Warren was instrumental in guiding NIAAA during the launch of a major NIH initiative: the Collaborative Research on Addiction at NIH, or CRAN. For his pivotal leadership, Dr. Warren received the NIH Director's Award in 2014 for "outstanding and sustained service to the National Institutes of Health and commitment to alcohol and addictions research."

Dr. Warren has also garnered numerous honors from the wider alcohol research community. He received the 1996 Seixas Award from the Research Society on Alcoholism (RSA) and the 2002 Henry Rosett Award from RSA's Fetal Alcohol Syndrome Study Group. In 2007, the National Organization on Fetal Alcohol Syndrome (NOFAS) inducted Dr. Warren into its Tom and Linda Daschle FASD Hall of Fame, and in 2008 he received the NOFAS Excellence Award. In 2014, Dr. Warren was honored with the RSA Lifetime Achievement Award.

Even after such a singular career, on the day following his retirement celebration, Dr. Warren was quietly back at work in a new role as Senior Advisor for Science and Operations, epitomizing his tireless dedication to NIAAA's mission to understand the impact of alcohol on human health and well-being.

"Dr. Warren has shown incredible dedication to NIAAA, and the impact of his many accomplishments will continue long after this transition into the next phase of his life."

—Dr. George Koob
NIAAA Director

on alcoholic beverage containers. In recognition of his critical role, Dr. Warren received the Public Health Service's Superior Service Award in 1982. He also helped to develop the updated advisory issued in 2005.

Throughout his NIAAA career, Dr. Warren has held many leadership roles. He was first a branch chief and then Deputy Director of the former Division

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alcohol over a lifetime than men. Breast cancer is another notable risk for women who drink alcohol. Women who consume about 1 drink per day have a 10 percent higher chance of developing breast cancer than women who do not drink at all. That risk rises another 10 percent for every additional drink they have per day.

New epidemiological analyses by NIAAA scientists, published in October 2015 in *Alcoholism: Clinical and Experimental Research*, indicate that women's drinking patterns are becoming more similar to men's. This observed increase in women's drinking rates makes women's greater risk for a variety of alcohol-related problems relative to men's risk all the more concerning.

In the study, researchers led by Aaron White, Ph.D., NIAAA's Senior Scientific Advisor to the Director, examined data from yearly national surveys conducted between 2002 and 2012. Dr. White and his colleagues found that, between 2002 and 2012, differences in measures such as current drinking, number of drinking days per month, reaching criteria for AUD, and driving under the influence of alcohol in the past year, all narrowed

for females and males. Males still consume more alcohol, but the differences between men and women are diminishing. For example, the percentage of people who drank alcohol in the previous 30 days increased for females from 44.9 percent to 48.3 percent, but decreased for males from 57.4 percent to 56.1 percent between 2002 and 2012. Over that time, the average number of drinking days in the past month also increased for females, from 6.8 days to 7.3 days, but decreased slightly for males, from 9.9 days to 9.5 days.

The changing patterns of alcohol consumption underscore the need for new data on the different biological and physiological effects that alcohol has on women and men, and coincide with an initiative, announced in May 2014 by NIH Director Francis S. Collins, M.D., Ph.D., to spur a revolution in cell and animal research. Noting that a current overreliance on male animals and lack of attention to the sex of cells can lead to neglect of key sex differences that should be guiding clinical studies and, ultimately, clinical practice, the NIH initiative aims to make sex-based

considerations and analyses as fundamental to preclinical studies as the inclusion of women in clinical studies has become since the early 1990s.

At NIAAA, Dr. Koob has directed the research divisions to develop study design proposals that are responsive to the new initiative. A new review article related to this topic, jointly authored by Drs. Jill Becker and George Koob and titled, "Sex Differences in Animal Models: Focus on Addiction," was published in the January 2016 issue of the journal *Pharmacological Reviews*. The article discusses ways to think about and study sex differences in preclinical animal models.

"We use the framework of addiction to illustrate the importance of considering sex differences," says Dr. Koob. "A better understanding of the ways males and females can differ will help scientists design experiments to better characterize the presence or absence of sex differences in new phenomena that they are investigating. We have outlined major quantitative, population, and mechanistic sex differences in the addiction domain, and we emphasize the need for new studies to help us understand those differences."

NOTEWORTHY

DR. PATRICIA POWELL APPOINTED ACTING DEPUTY DIRECTOR



As of November 2015, Patricia A. Powell, Ph.D., has been serving as Acting Deputy Director of NIAAA. She was appointed after the retirement of Kenneth R. Warren, Ph.D., who served as

both Acting Director and Deputy Director during the course of his 39-year career at NIAAA. Previously, Dr. Powell held the position of NIAAA Associate Director for Scientific Initiatives, a role

in which she oversaw a broad range of research activities, sought opportunities to jumpstart or expand projects that reflect the Director's priorities, and identified opportunities for NIAAA to become more involved in existing activities and initiatives across NIH, the U.S. Department of Health and Human Services, and beyond.

Prior to that, Dr. Powell served as Chief of the NIAAA Science Policy Branch. She joined NIAAA as an American Association for the Advancement of Science (AAAS) fellow at the National Science Foundation, focusing on bringing cutting-edge science to the public through science museums, television and radio programs, and IMAX films.

At NIAAA, Dr. Powell has been actively involved in many aspects of

underage drinking prevention. She served as one of two scientific editors for *The Surgeon General's Call to Action To Prevent and Reduce Underage Drinking*, and she worked closely with the Leadership to Keep Children Alcohol Free Initiative, spearheaded by spouses of current and former Governors and focused on the prevention of drinking by children ages 9–15.

Dr. Powell has 20 years of research experience in developmental genetics and cellular and molecular biology. She received her Ph.D. in cellular and molecular biology from Washington University in St. Louis and, following that, did postdoctoral studies at the Salk Institute, the University of California at San Diego, and Washington University in St. Louis.

SPOTLIGHT

MAJOR STUDY WILL HELP DEFINE HOW SUBSTANCE USE AFFECTS ADOLESCENT BRAIN DEVELOPMENT



In September 2015, NIH launched a groundbreaking national study of how substance use affects brain development in the short and long term. The Adolescent Brain Cognitive Development (ABCD) Study will follow about 10,000 children beginning at ages 9–10, before they start using any drugs, for 10 years into early adulthood.

ABCD Study investigators will use advanced brain imaging and a range of psychological and behavioral research tools to delineate how occasional or regular use of alcohol, marijuana, nicotine, and other substances affects adolescent brain structure and function, mental health, cognitive skills, and academic achievement.

The ABCD Study was initiated by the Collaborative Research on Addiction at NIH (CRAN), a partnership between NIAAA, the National Institute on Drug Abuse, and the National Cancer Institute. Other NIH collaborators in this project are the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development, the

National Institute of Mental Health, the National Institute on Minority Health and Health Disparities, the National Institute of Neurological Disorders and Stroke, and the Office of Behavioral and Social Sciences Research.

For more information about the ABCD Study, see:

- Adolescent Brain Cognitive Development Study, Collaborative Research on Addiction at NIH (<http://addictionresearch.nih.gov/adolescent-brain-cognitive-development-study>)
 - NIH Launches Landmark Study on Substance Use and Adolescent Brain Development, NIH News Release, September 25, 2015 (<http://www.nih.gov/news-events/news-releases/nih-launches-landmark-study-substance-use-adolescent-brain-development>)
 - NIAAA and Other NIH Institutes Propose Major Study of Substance Use on Adolescent Brain Development, *NIAAA Spectrum*, September 2014 (<http://www.spectrum.niaaa.nih.gov/archives/V6I3Sep2014/features/Features02.html>)
- Two ABCD Study grants will support a coordinating center and a data center at the University of California, San Diego, while 11 grants will fund ABCD research at the following sites:
- Children’s Hospital of Los Angeles, CA
 - Florida International University, Miami, FL
 - Laureate Institute for Brain Research, Tulsa, OK
 - Neurobehavioral Research, Inc., Wailuku, HI
 - Oregon Health & Science University, Portland, OR
 - SRI International, Arlington, VA
 - Icahn School of Medicine at Mount Sinai, New York, NY
 - University of California, Los Angeles, CA
 - University of California, San Diego, CA
 - University of Colorado, Boulder, CO
 - University of Florida, Gainesville, FL
 - University of Hawaii at Manoa, HI
 - University of Michigan, Ann Arbor, MI
 - University of Minnesota, Minneapolis, MN
 - University of Pittsburgh, PA
 - University of Utah, Salt Lake City, UT
 - University of Vermont, Burlington, VT
 - Virginia Commonwealth University, Richmond, VA
 - Washington University, St. Louis, MO
 - Weill Medical College at Cornell University, New York, NY

A CLOSER LOOK

NIAAA RELEASES *CollegeAIM*

With the release of the *CollegeAIM* (which stands for College Alcohol Intervention Matrix) print guide and Web site in September 2015, NIAAA has embarked on an ambitious promotional effort that included several high-profile presentations. Top, NIAAA Director Dr. George F. Koob joined Dr. Jonathan Gibralter, President of Wells College and Chair of the NIAAA Working Group to Address Harmful and Underage Student Drinking, to announce the release of *CollegeAIM* via Webcast from the National Press Club in Washington, D.C. Bottom, Dr. Koob discussed *CollegeAIM* at a Congressional briefing on Capitol Hill, sponsored by the Friends of NIAAA in cooperation with the Congressional Addiction, Treatment, and Recovery Caucus. Additional promotional activities will include school-hosted regional workshops, presentations at professional conferences for college staff, and social media activities.

The result of a multiyear collaboration, *CollegeAIM* is an easy-to-use and comprehensive resource to help schools address harmful and underage student drinking by directing them to effective, evidence-based intervention strategies. For more information, visit <http://www.CollegeDrinkingPrevention.gov/CollegeAIM>.



New From NIAAA—*CollegeAIM* Guide and Web Site



How is *CollegeAIM* different?

CollegeAIM is distinctive because of the breadth of its research and analysis, the expertise of its contributors, and its user-friendly format:

- Extensive review of decades of scientific literature
- Multiyear collaboration involving 16 leaders in college alcohol intervention research
- Nearly 60 interventions rated for effectiveness, costs, and other criteria
- Two **user-friendly** matrices and other resources

What is *CollegeAIM* and why is it needed?

The College Alcohol Intervention Matrix is a new resource to help schools address harmful and underage student drinking.

Developed with leading college alcohol researchers and staff, it is an **easy-to-use** and **comprehensive** tool to identify effective alcohol interventions.

While there are numerous options for addressing alcohol issues, they are not all equally effective.

CollegeAIM can help schools **choose interventions wisely**—helping them improve the health and safety of their students.

How can schools use *CollegeAIM*?

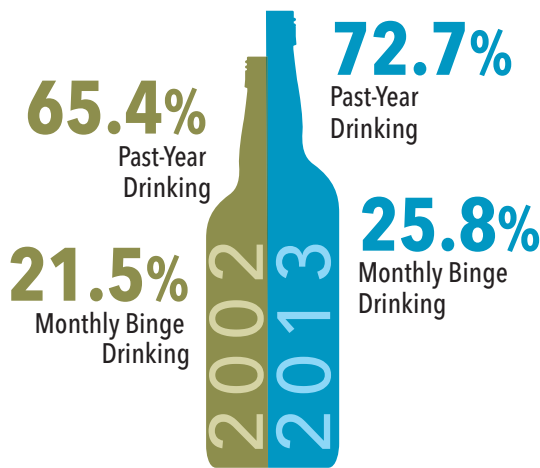
With the help of *CollegeAIM*, school officials can:

- Learn how their current strategies compare to other alternatives
- Find new evidence-based options
- Use the **interactive strategy planning worksheet** to help select a combination of approaches that meets the needs of their campus and their budget

Visit www.collegedrinkingprevention.gov/CollegeAIM

NEWS FROM THE FIELD

NESARC–III: ADULTS ARE DRINKING MORE ALCOHOL THAN A DECADE AGO



Adults drank more alcohol in 2012–2013 than they did in 2001–2002, according to the most recent National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). NESARC–III is a cross-sectional survey

sponsored, designed, and directed by NIAAA and is the largest study ever conducted on the co-occurrence of alcohol use, drug use, and related psychiatric conditions.

To assess how drinking patterns have changed over time, researchers compared the NESARC–III data with that from Wave 1 NESARC. In both surveys, which had similar objectives and content areas, researchers assessed a large sample of U.S. adults through personal interviews conducted in participants’ homes. However, unlike Wave 1 NESARC, NESARC–III researchers collected saliva samples from participants for future DNA analyses.

Data analysis revealed that between 2001–2002 and 2012–2013, past-year drinking prevalence increased from 65.4 percent to 72.7 percent, and the

prevalence of monthly binge drinking increased from 21.5 percent to 25.8 percent. Likewise, overall frequency of drinking increased from 83.5 days per year to 87.9 days per year. The authors of the study observed that these statistics, along with the increase in daily alcohol consumption (from 0.628 ounces to 0.751 ounces), indicate “a wetter drinking climate.”

One particularly striking finding was that African Americans experienced disproportionate increases in past-year drinking prevalence (from 53.2 percent to 66.1 percent) and past-month binge drinking prevalence (from 19 percent to 27.7 percent), as well as average daily volume (from 0.751 ounces to 1.033 ounces), compared with Caucasians. The authors suggest this

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NEWS FROM THE FIELD

BRIEF TRAINING INCREASES PEDIATRICIANS’ USE OF SUBSTANCE ABUSE AND MENTAL HEALTH INTERVENTIONS



Two to three brief training sessions can significantly increase pediatricians’ use of screening and brief interventions to help their patients with substance use and mental health problems, according to a large, 2-year trial supported by NIAAA. The study also found that

pediatric practices can increase delivery of these services by adding behavioral health clinicians to their teams.

Mounting evidence supports the use of screening, brief intervention, and referral to treatment (SBIRT) in pediatric practices to reduce underage drinking and its harmful consequences. Pediatricians often report barriers to conducting SBIRT, however, including time constraints and a lack of training.

Researchers at Kaiser Permanente Northern California compared two practical ways to overcome these barriers and increase the delivery of SBIRT services in a trial involving about 50 pediatricians and 1,900 adolescents.

One group of pediatricians was offered three 60-minute SBIRT training sessions then encouraged to conduct assessments and brief interventions when needed. A second group had one 60-minute training session, then was encouraged to assess and refer patients as needed for interventions by clinical psychologists “embedded” in their practices. For comparison, a third, “usual care” group had access to the same clinical guidelines and tools but no SBIRT training or psychologists in their practices.

The researchers found that, following SBIRT training, the pediatrician-only group was about 10 times more likely to conduct brief interventions with

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NEWS FROM THE FIELD

PREVALENCE OF MARIJUANA USE AMONG U.S. ADULTS DOUBLES OVER PAST DECADE



The percentage of Americans who reported using marijuana in the past year more than doubled between 2001–2002 and 2012–2013, and the increase in marijuana use disorder during that time was nearly as large. Past-year marijuana use rose from 4.1 percent to 9.5 percent of the U.S. adult population, while the prevalence of marijuana use disorder rose from 1.5 percent to 2.9 percent, according to national surveys conducted by NIAAA. This translates to 30 percent of marijuana users meeting the criteria for marijuana use disorder.

Marijuana use disorder includes symptoms such as taking the drug in larger

amounts or over a longer period than was intended by the user; the persistent desire to cut down or control use/ unsuccessful efforts to do so; failure to fulfill major role obligations at work, school, or home as a result of marijuana use; and tolerance and/or withdrawal.

“Based on the results of our surveys, marijuana use in the United States has risen rapidly over the past decade, with about 3 in 10 people who use marijuana meeting the criteria for a marijuana use disorder. Given these increases, it is important that the scientific community convey information to the public about

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NEWS FROM THE FIELD

CLINICAL COURSE OF ALCOHOL USE DISORDER IN YOUNG ADULT NATIVE AND MEXICAN AMERICANS



In a recent study, Cindy L. Ehlers, Ph.D., and colleagues examined the clinical course of alcohol use disorder (AUD)—as defined by the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM–5)—in a sample of young adult (ages 18–30) individuals of Mexican American (MA) and Native American (NA) descent.

Face-to-face interviews using the Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) were conducted with 619 MA and 510 NA community-based participants recruited in southwest California. Of the total sample of 1,129 participants, 634 (56

percent) met criteria for a lifetime diagnosis of DSM–5 AUD. Mild AUD was found in 22 percent of participants, moderate AUD in 14 percent, and severe AUD in 20 percent. Further data analysis revealed that 70 percent of the NA men, 64 percent of the NA women, 56 percent of the MA men, and 42 percent of the MA women met the lifetime diagnostic criteria for AUD.

The researchers examined the clinical course of AUD, as defined by order and progression of 36 alcohol-related life events, within their MA and NA young adult sample. A comparison of these alcohol-related life experiences and their order of occurrence over time was made between male and female and between MA and NA participants. NAs reported more alcohol-related life events and at an earlier age than MAs. Otherwise, a high degree of similarity in clinical course was found between men and women and between MA and NA individuals. The researchers also analyzed their data across severity of DSM–5 AUD disorder (mild, moderate,

or severe). The high degree of similarity in the clinical course for moderate and severe AUD and across genders was not found for mild AUD. This information suggests that mild AUD may not be part of the same clinical continuum as moderate and severe AUD for NA and MA populations.

It should be noted that this study was limited by the specificity of the participant sample, which means the results may not be generalizable to the population as a whole. However, the findings are significant because they are informative for understanding health disparities in the groups studied and because they provide some early insights into the new DSM–5 mild, moderate, and severe AUD categories.

Source:

Ehlers, C.L.; Stouffer, G.M.; Corey, L.; and Gilder, D.A. The clinical course of DSM-5 alcohol use disorders in young adult native and Mexican Americans. *American Journal of Addiction* 24(8):713–721, 2015. PMID: 26346282

NEWS FROM THE FIELD: NESARC-III . . . Continued from page 6

may indicate disparities in treatment availability and/or treatment seeking.

Another notable finding was that percent increases in prevalence and overall drinking frequency were about twice as high for women as for men, prior to adjustment for sociodemographic differences. Adjusting for these differences, women demonstrated larger increases than men in all

consumption measures. According to the authors, this finding may contribute to evidence of a closing gender gap in heavy drinking.

Looking ahead, scientists will continue to analyze the various waves of NESARC data to advance our understanding of drinking trends through comparison of survey results over time.

Source:

Dawson, D.A.; Goldstein, R.B.; Saha, T.D.; and Grant, B.F. Changes in alcohol consumption: United States, 2001-2002 to 2012-2013. *Drug and Alcohol Dependence* 148:56-61, 2015. PMID: 25620731

NEWS FROM THE FIELD: Brief Training . . . Continued from page 6

patients deemed at risk, compared with usual care pediatricians (16 percent for the trained group vs. 1.5 percent for usual care). In the pediatrician-plus-psychologist group, 24 percent of at-risk patients received brief interventions.

Although overall pediatrician attention to behavioral health concerns was still

low following training, the researchers indicated that embedding behavioral health clinicians in primary care could be a cost-effective way to increase SBIRT delivery. Future analyses will examine patient outcomes and the cost-effectiveness of the two SBIRT delivery options.

Source:

Sterling, S.; Kline-Simon, A.H.; Satre, D.D.; Jones, A.; Mertens, J.; Wong, A.; and Weisner, C. Implementation of screening, brief intervention, and referral to treatment for adolescents in pediatric primary care: A cluster randomized trial. *JAMA Pediatrics* 169(11):e153145, 2015. PMID: 26523821

NEWS FROM THE FIELD: Marijuana . . . Continued from page 7

the potential harms,” said George F. Koob, Ph.D., Director of NIAAA.

Data about marijuana use were collected as part of NIAAA’s National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). In total, 79,000 people were interviewed on alcohol use, drug use, and related

psychiatric conditions during the 2001–2002 and 2012–2013 surveys.

The study authors note that public education about the dangers associated with marijuana use, presented in a reasonable and balanced manner, will be increasingly important to counteract the perception that marijuana use is harmless.

Source:

Hasin, D.S.; Saha, T.D.; Kerridge, B.T.; Goldstein, R.B.; Chou, S.P.; Zhang, H.; Jung, J.; Pickering, R.P.; Ruan, W.J.; Smith, S.M.; Huang, B.; and Grant, B.F. Prevalence of marijuana use disorders in the United States between 2001-2002 and 2012-2013. *JAMA Psychiatry* 72(12): 1235-1242, 2015. PMID: 26502112

ABOUT US

NIAAA Spectrum is NIAAA’s Webzine. With engaging feature articles, short news updates, and colorful graphics, *NIAAA Spectrum* offers accessible and relevant information on NIAAA and the alcohol research field for a wide range of audiences.

Each issue includes feature-length stories, new research findings from the field, image and data analyses, and an interview with an NIAAA staff member or alcohol researcher. *NIAAA Spectrum* is published three times a year.

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